#11

MORRISON & FOERSTER

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NEW YORK
WASHINGTON, D.C.
DENVER
LONDON
BRUSSELS
HONG KONG
TOKYO

November 22, 1995

DIRECT DIAL NUMBER

(415) 813-5730

By Messenger

Mr. Gerald Dost
U.S. Patent and Trademark Office
Patent Term Extension Application Branch
Washington, D.C. 20231

Re: New U.S. Patent Application
For: Application for Patent Term Extension for U.S. Patent No. 4,983,395
By: Yunik Chang
Our reference: 29065-28024.00

Dear Mr. Dost:

Enclosed is an Application for Patent Term Extension for Patent No. 4,983,395, including a certified copy of the application, three working copies, transmittal letter, check in the amount of $1,060.00, and postcard. The sixty day statutory deadline expires for this application on **November 28, 1995.** If you have any questions or comments, please contact me at the above number.

Sincerely,

Antoinette

Antoinette F. Konski

Enclosures

111-1060.00 DAJC for PPP

PATENT #11
Docket No. 290652802400

CERTIFICATE OF HAND DELIVERY

I hereby certify that this correspondence is being hand filed with the United States Patent and Trademark Office in Washington, D.C. on November 24 1995.

Signature: Annette Masiello

PRINTED NAME:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Yunik Chang et al.

Serial No.: 07/326,536

Filing Date: March 21, 1989

Patent No.: 4,983,395

Issued: January 8, 1991

For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

Sir:

TRANSMITTAL LETTER

Assistant Commissioner for
Patents and Trademarks
Box Patent Extension
Washington, D.C. 20231

Enclosed are the following:

1. Application for Extension of Patent Term Under 35 U.S.C. Section 156.

2. A Certified Duplicate Application for Extension of Patent Term Under 35 U.S.C. Section 156.

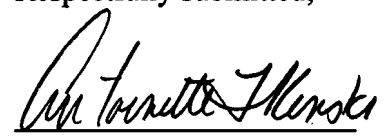
140 AA 11/28/95 07326536 1 111 1,060.00 CK

3. Three (3) Working Copies of Application for Extension of Patent Term Under 35 U.S.C. Section 156.

4. A check in the amount of $1,060.00.

In the unlikely event that this transmittal letter is separated from this document and the Patent Office determines that an additional fee is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing these papers to Deposit Account No. 03-1952.

Respectfully submitted,



Antoinette F. Konski
Registration No. 34,202

Date: November 22, 1995

MORRISON & FOERSTER
755 Page Mill Road
Palo Alto, CA 94304-1018
(415) 813-5600
Fax: (415) 494-0792

PATENT
Docket No. 290652802400

CERTIFICATE OF HAND DELIVERY

I hereby certify that this correspondence is being hand filed with the United States Patent and Trademark Office in Washington, D.C. on November 24, 1995.

Singed:_____

Printed Name:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Yunik Chang et al.

Serial No.: 07/326,536

Filing Date: March 21, 1989

Patent No.: 4,983,395

Issued: January 8, 1991

For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. SECTION 156

Assistant Commissioner for Patents
Box Patent Extension
Washington, D.C. 20231

Dear Sir:

In accordance with 35 U.S.C. Section 156, Applicant TheraTech, Inc. a corporation of the State of Delaware, having a place of business at 417 Wakara Way, Suite 100, Salt Lake City, Utah, 84108, (hereinafter "TheraTech") represents that it is the assignee of the entire interest in and to Letters Patent of the United States No. 4,983,395, granted to Yunik Chang, Dinesh C. Patel, and Charles D. Ebert for DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA by virtue of an assignment in favor of TheraTech, recorded on March 21, 1989, on Reel

5056, Frame 0212, and by virtue of an assignment for U.S. Patent No. 4,849,224, filed November 12, 1987, directed to DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA, recorded on December 28, 1987, on Reel 4802, Frame 0996. See Appendix Tab A for copies of the assignment documents identified above.

This application is submitted by Applicant's authorized agent as set forth in 37 C.F.R. Section 1.730. See Appendix Tab B for a copy of the Power of Attorney authorizing the undersigned to act in this manner. Applicant hereby submits this application for extension of patent term under 35 U.S.C. Section 156 by providing the following information as set forth in 37 C.F.R. Section 1.740.

(1) The approved product is identified as Androderm® that is used for the transdermal administration of testosterone.

(2) The approved product was subject to regulatory review under Section 505(b) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. Section 360(e)).

(3) The approved product received permission for commercial marketing and use under Section 505(b) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. Section 360(e)) on September 29, 1995.

(4) This Application for extension of the patent term under 35 U.S.C. Section 156, is being submitted within the statutory 60 day period, said period to expire on November 28, 1995.

(5) The complete identification of the patent for which extension is being sought is as follows:

Inventors: Yunik Chang, Dinesh C. Patel, and Charles D. Ebert

Patent No.: 4,983,395

Issue Date: January 8, 1991

Expires: July 18, 2006 (17 year patent term minus the term lost due to terminal disclaimer) or November 12, 2007 (20 years from the earliest filing date claimed under 35 U.S.C. Section 120).

(6) See Appendix Tab C for a copy of the patent identified in Paragraph 5, above.

(7) A receipt of maintenance fee payment has been issued with regard to U.S. Patent No. 4,983,395. A copy of the maintenance fee receipt is attached as Appendix Tab D.

(8) A copy of the terminal disclaimer filed in connection during the prosecution of U.S. Patent No. 4,983,395 is attached as Appendix Tab E. No reexamination certificate or Certificate of Correction has been issued in connection with U.S. Patent No. 4,983,395.

STATEMENT PURSUANT TO 37 C.F.R. 1.740(a)(9)

(9) U.S. Patent No. 4,983,395, claims the approved product Androderm®. The product is manufactured as a closed system that when opened, is ready for application by a patient. The product consists of a gel reservoir, that is formed between an impermeable backing film and a microporous membrane. The gel reservoir contains the active agent --testosterone and skin permeation enhancers. On one side of the reservoir is an active agent impermeable, ethylene vinyl acetate copolymer/polyester laminate backing film. On the opposite side of the reservoir are several layers. The first layer lies adjacent to the reservoir; it is a microporous membrane. Adjacent to the microporous membrane is a peelable disk that serves to isolate the reservoir gel from the reservoir from the adhesive. The peel-seal disk provides product stability by preventing migration of the reservoir gel components into the peripheral adhesive over prolonged storage. The pressure sensitive adhesive layer is positioned below and around the periphery of the peelable disk. A second, separate adhesive layer is positioned directly below the peelable disk layer. The final layer is the release liner.

Claims 1 through 6 describe a device for administering an active agent such as testosterone (column 5, lines 14 and 15, of the patent) to the skin or mucosa of an individual. Claims 1 through 3, embrace the product Androderm®. The manner in which each applicable patent claim reads on the approved product is as follows:

Claim 1 of U.S. Patent No. 4,983,395, claims a laminated composite comprising:

a) a backing layer;

b) an active agent-permeable membrane, the backing and membrane defining

c) a reservoir therebetween that contains a formulation of the active agent, said reservoir having a smaller periphery than the backing layer and membrane such that a portion of the backing layer and membrane extends outwardly of the periphery of the reservoir;

d) a first peelable active agent formulation-impermeable layer that underlies the reservoir and a portion of said outwardly extending portion of the backing layer and membrane;

e) an adhesive layer that underlies and covers the first peelable active agent formulation-impermeable layer and said outwardly extending portion of the backing layer and membrane;

f) a second peelable active agent formulation-impermeable layer that underlies and covers the adhesive layer;

g) a permanent heat seal about the periphery of the reservoir between the backing layer and the membrane; and

h) a peelable heat seal between the membrane and the first peelable active agent formulation-impermeable layer located underneath and at a radius not less than that of the permanent heat seal, said permanent and peelable heat seals providing barriers to migration of components of the active agent formulation from the reservoir into the adhesive layer and said first and second peelable active agent impermeable layers being bonded together such that when the second peelable layer is removed from the device, the peelable heat seal is broken and the first peelable layer and underlying portion of the adhesive layer is removed therewith.

Androderm® contains a backing layer (element (a) of claim 1), the microporous membrane lying below and defining the gel reservoir (element (b) of claim 1), the reservoir into which the active agent testosterone and permeation enhancers are initially loaded (element (c) of claim 1), a first peelable active agent formulation-impermeable layer that underlies the reservoir that lies underneath the reservoir which extends beyond the periphery of the reservoir (element (d) of claim 1), an adhesive layer that lies underneath the first peelable active agent formulation (element (e) of claim 1), a release liner that serves as a second peelable active agent formulation-impermeable layer that underlies and covers the adhesive layer (element (f) of claim 1), two heat seals, the first heat seal between the membrane and the first peelable active agent-impermeable

layer (element (h) of claim 1) and the second about the periphery of the reservoir (element (g) of claim 1). Therefore, claim 1 embraces Androderm®.

Claim 2 of U.S. Patent No. 4,983,395, is to the device of claim 1, wherein the adhesive is incompatible with one or more of the components of the formulation that permeate through and an inner heat-sealable layer. Pressure sensitive adhesives used in transdermal application are not stable in contact with permeation enhancers, and do become plasticized and ineffective. Thus, the pressure sensitive adhesive utilized around the periphery of the reservoir to adhere the device to the skin is incompatible with the permeation enhancer in the formulation initially loaded into the reservoir. Thus, Androderm® embraces claim 2 of U.S. Patent No. 4,983,395.

Claim 3 claims the device of claim 1 wherein the backing layer is a laminated composite of at least one layer that is impermeable to the formulation and an inner heat sealable layer. Androderm® contains the peel seal disc that is impermeable to the formulation and an inner heat sealable layer. Therefore, claim 3 embraces the product Androderm®.

STATEMENT PURSUANT TO 37 C.F.R. SECTION 1.740(a)(10)

(10) The relevant dates and information pursuant to 35 U.S.C. Section 156(g), to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

(a) As shown in Appendix Tab F, the application under subsection (i) of Section 505(b) of the Federal Food, Drug and Cosmetic Act for an Investigational New Drug Application for Androderm® was received on November 28, 1989. Receipt was acknowledged on December 1, 1989.

(b) As shown in Appendix Tab F, the date the application with respect to the human drug product under Section 505(b) of the Federal Food, Drug, and Cosmetic Act was received September 30, 1994.

(c) The application was approved by the Food and Drug Administration on September 29, 1995.

STATEMENT PURSUANT TO 37 CFR §1.740(a)(11)

(11) As a brief description of the activities undertaken by the marketing applicant, TheraTech, during the applicable regulatory review period as set forth in 37 CFR §1.740(a)(11), is set forth in Appendix Tab F, as a chronology of the major communications between TheraTech and the FDA from about November 28, 1989 until about September 29, 1995.

STATEMENT PURSUANT TO 37 CFR §1.740(a)(12)

(12) Applicant is of the opinion that U.S. Patent No. 4,893,395, is eligible for extension under 35 U.S.C. Section 156, whether patent term is measured seventeen (17) years from date of issue minus any term disclaimed or twenty (20) years from the earliest filing date claimed under 35 U.S.C. Section 120, because it satisfies all the requirements for such extensions as follows:

(a) 35 U.S.C. Section 156(a)

U.S. Patent No. 4,893,395, claims a drug delivery device embodied by Androderm®.

(b) 35 U.S.C. Section 156(a)(1)

The term of U.S. Patent No. 4,983,395, has not expired before submission of this application.

(c) 35 U.S.C. Section 156(a)(2)

The term of U.S. Patent No. 4,983,395, has never been extended.

(d) 35 U.S.C. Section 156(a)(3)

The application for extension is submitted by TheraTech, the assignee of the entire interest of U.S. Patent No. 4,983,395. See Appendix Tab A.

(e) 35 U.S.C. Section 156(a)(4)

The product, Androderm® has been subject to a regulatory review period before its commercial marketing or use.

(f) 35 U.S.C. Section 156(a)(5)(a)

The commercial marketing or use of the product, Androderm® after the regulatory review period is the first permitted commercial marketing or use of the product under the provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. Section 355) under which such regulatory period occurred.

(13) The length of extension of the patent term of U.S. Patent No. 4,983,395, claimed by TheraTech is 2.25 years or 820 days. The length of the extension was determined as follows:

(a) The regulatory review period under 35 U.S.C. Section 156(g)(3)(A) as set forth in 37 CFR Section 1.775, is sum of: a) the period beginning on the date an exemption under subsection (i) of Section 505 of the Federal Food, Drug, and Cosmetic Act became effective for the approved product and ending on the date the application was initially submitted for such product; and b)the number of days in the period beginning on the date the application was initially submitted for the approved product under Section 351 of the Public Health Service Act, subsection (b) of the Federal Food, Drug, and Cosmetic Act and ending on the date such application was approved under such Section. The applicable number of days for Androderm® for this period is 2101 days or 5.8 years, which began on November 28, 1989 and ending about September 29, 1995.

(b) The regulatory review period upon which the period of extension is calculated is the entire regulatory review period as determined in sub-paragraph 13(a) above (365 days) less the sum of:

(i) The number of days in the regulatory period as set forth in §1.775(c)(1) and (2) which were on and before the date on which the patent issued, which is 461 days (i.e., from November 28, 1989 to January 8, 1991);

(ii) The number of days in the regulatory period as set forth in §1.775(c)(1) and (2) during which TheraTech, did not act with due diligence, which is zero (0) days (365 - 0 = 365); and

(iii) One-half the number of days remaining in the period as set forth in §1.775(c)(1) after that period is reduced in accordance with paragraphs (d)(1)(i) and (ii), which is (1640 ÷ 2 = 820 days or 2.25 years);

(c) The number of days as determined in 13(b) above, that is, 820 days or 2.25 years, when added to the original term of the patent that is July 18, 2006 or November 12, 2007, would result in the date October 16, 2008 or February 10, 2009, respectively.

(d) The addition of fourteen (14) years to the date of approval of the application under Section 351 of the Federal Food, Drug and Cosmetic Act would result in the date September 29, 2009.

(e) When comparing 13(c) and (d) above, the earlier date is either of October 16, 2008 or February 10, 2009.

(f) Since the original patent issued after September 24, 1984, and since no request for exemption under subsection (i) of §505 of the Federal Food, Drug and Cosmetic Act was submitted before September 24, 1984, five (5) years when added to the original expiration date of the patent would result in the dates of July 18, 2011 (17 year patent term) or November 12, 2012 (20 year patent term).

(g) The earlier date when comparing 13(c) and (f) above is either of October 16, 2008 or February 10, 2009.

Therefore, the length of extension of patent term claimed by TheraTech is 820 days or 2.25 years.

STATEMENT PURSUANT TO 37 CFR §1.740(a)(13)

(14) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to any determinations to be made relative to the application for extension.

(15) The prescribed fee for receiving and acting upon this application is enclosed. If any additional fees are due, authorization is given to charge our deposit account number 03-1952.

(16) Direct all inquiries and correspondence relating to this application to

Antoinette F. Konski

Morrison & Foerster
755 Page Mill Road
Palo Alto, CA 94304
Phone: (415) 813-5730
Fax: (415) 494-0792

(17) A certified duplicate of this application is being submitted herewith.

(18) The requisite declaration pursuant to 37 CFR §1.740(b) is attached hereto as Appendix Tab G.

Respectfully submitted,

By: 
Antoinette F. Konski
Registration No.:34,202

Date: November 22, 1995

Morrison & Foerster
755 Page Mill Road
Palo Alto, CA 94304-1018
(415) 813-5600
Fax: (415) 494-0792

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

A

TO: IRELL & MANELLA
545 MIDDLEFIELD ROAD, STE. 200
MENLO PARK, CA 94025-3471

OCT 6 1989
RECEIVED

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE U.S. PATENT AND TRADEMARK OFFICE ON THE REEL AND FRAME NUMBER REFERENCED BELOW. A DIGEST OF THE DOCUMENT HAS ALSO BEEN MADE AND APPEARS IN THE OFFICE'S RECORDS AS SHOWN:

ASSIGNOR: 001 CHANG, YUNIK DOC DATE: 03/17/89
ASSIGNOR: 002 PATEL, DINESH C. DOC DATE: 03/16/89
ASSIGNOR: 003 EBERT, CHARLES D. DOC DATE: 03/16/89

RECORDATION DATE: 03/21/89 NUMBER OF PAGES 001 REEL/FRAME 5056/0212

DIGEST: ASSIGNMENT OF ASSIGNORS INTEREST

ASSIGNEE: 501 THERATECH, INC., RESEARCH PARK, 410 CHIPETA WAY, STE. 219 , SALT LAKE CITY, UT 84108, A CORP. OF UT

SERIAL NUMBER 7-326536 FILING DATE 03/21/89
PATENT NUMBER ISSUE DATE 00/00/00

TITLE OF INVENTION: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SK IN OR MUCOSA

INVENTOR: 001 CHANG, YUNIK
INVENTOR: 002 PATEL, DINESH C.
INVENTOR: 003 EBERT, CHARLES D.

DOCKETED TEC
9065-0003 20

Application for Patent Extension
Patent No. 4,983,395
Atty Dkt.: 290652802400
Appendix A

#702 578

Attorney Docket No. 9065-0003.2

IRELL & MANELLA
545 Middlefield Road, Suite 200
Menlo Park, California 94025-3471

07/326536

APPLICATION TRANSMITTAL LETTER

Honorable Commissioner of Patents and Trademarks
Washington, D. C. 20231

Sir:

Transmitted herewith for filing is the patent application

of Yunik Chang, Dinesh C. Patel, Charles D. Ebert

for DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

Enclosed are:

- [X] 2 sheet(s) of [ ] formal [X] informal drawing(s). (3 sets)
- [ ] A claim for foreign priority under 35 U.S.C. §119/363 in
  - [ ] a separate document [ ] the declaration.
- [ ] A certified copy of the priority document.
- [ ] An Associate Power of Attorney.
- [ ] _____ verified statement(s) of small entity status.

The declaration of the inventor [X] is enclosed [ ] will follow.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
Express Mail" Mailing Label No. MB190159775
Date of Deposit 3-21-89
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

DOROTHY M. PAUL
(Typed or Printed Name of Person Mailing Paper or Fee)

Dorothy M. Paul
(Signature of Person Mailing Paper or Fee)

The fee has been calculated as follows:

A.	Basic Application Fee		$ 340.00
B.	Total Claims 6 minus 20 = 0 x $ 12.00	=	$ -0-
C.	Independent Claims 1 minus 3 = 0 x $ 34.00	=	$ -0-
D.	If multiple dependent claims present, add $ 110.00	=	$ -0-
E.	Total Application Fee (Total of A, B, C, & D)	=	$ 340.00
F.	If verified statement of small entity status is enclosed, fifty percent reduction of Total Application Fee (50% x E)	=	$ -0-
G.	Application Fee Due (E minus F)	=	$ 340.00
H.	Assignment Recording Fee of $7.00 if assignment document enclosed.	=	$ 7.00
I.	TOTAL FEE (G plus H)	=	$ 347.00

[X] A check in the amount of $ 347.00 is attached.

[ ] Charge $ _____ to Deposit Account No. 03-1952.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 03-1952. A duplicate copy of this sheet is enclosed.

*Attention: Assignment Branch

1 518 7.00 CK

93032427

By Thomas E. Ciotti
Thomas E. Ciotti
Registration No.: 21,013

Phone No.: 415/327-7250

Attorney Docket No. 9065-0003.20

ASSIGNMENT

JOINT

THIS ASSIGNMENT, by * Yunik Chang, Dinesh C. Patel, Charles D. Ebert,

(hereinafter referred to as the assignors), residing at Toms River, New Jersey; Murray, Utah; Salt Lake City, Utah and Salt Lake City, Utah

respectively, witnesseth:

WHEREAS, the said assignors have invented certain new and useful improvements in DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

set forth in an application for Letters Patent of the United States, [X] having an oath or declaration executed on even date herewith; [ ] bearing Serial No. _____ and filed on _____ ; and

WHEREAS, TheraTech, Inc., a corporation duly organized under and pursuant to the laws of Utah, and having its principal place of business at Research Park, 410 Chipeta Way, Suite 219, Salt Lake City, Utah 84108

(hereinafter referred to as the assignee) is desirous of acquiring the entire right, title and interest in and to said inventions and said application for Letters Patent of the United States, and in and to any Letters Patent or Patents, United States or foreign, to be obtained therefor and thereon:

NOW THEREFORE, in consideration of one Dollar ($ 1.00) and other good and sufficient considerations, the receipt of which is hereby acknowledged, the said assignors have sold, assigned, transferred and set over, and by these presents do sell, assign, transfer and set over, unto the assignee, its successors, legal representatives and assigns, the entire right, title and interest in and to the abovementioned inventions, application for Letters Patent, and any and all Letters Patent or Patents in the United States of America and all foreign countries which may be granted therefor and thereon, and in and to any and all divisions, continuations, and continuations-in-part of said application, or reissues or extensions of said Letters Patent or Patents, and all rights under the International Convention for the Protection of Industrial Property, the same to be held and enjoyed by the said assignee, for its own use and behoof and the use and behoof of its successors, legal representatives and assigns, to the full end of the term or terms for which Letters Patent or Patents may be granted, as fully and entirely as the same would have been held and enjoyed by the assignors, had this sale and assignment not been made.

AND for the same consideration, the said assignors hereby covenant and agree to and with the said assignee, its successors, legal representatives and assigns, that, at the time of execution and delivery of these presents, the said assignors are the sole and lawful owners of the entire right, title and interest in and to the said inventions and the application for Letters Patent abovementioned, and that the same are unencumbered and that the said assignors have good and full right and lawful authority to sell and convey the same in the manner herein set forth.

AND for the same consideration, the said assignors hereby covenant and agree to and with the said assignee, its successors, legal representatives and assigns, that the said assignors will, whenever counsel of the said assignee, or the counsel of its successors, legal representatives and assigns, shall advise that any proceeding in connection with said inventions, or said application for Letters Patent, or any proceeding in connection with Letters Patent for said inventions in any country, including interference proceedings, is lawful and desirable, or that any division, continuation or continuation-in-part of any application for Letters Patent, or any reissue or extension of any Letters Patent, to be obtained thereon, is lawful and desirable, sign all papers and documents, take all lawful oaths, and do all acts necessary or required to be done for the procurement, maintenance, enforcement and defense of Letters Patent for said inventions, without charge to the said assignee, its successors, legal representatives and assigns, but at the cost and expense of the said assignee, its successors, legal representatives and assigns.

AND the said assignors hereby request the Commissioner of Patents to issue said Letters Patent of the United States to the said assignee as the assignee of said inventions and the Letters Patent to be issued thereon for the sole use and behoof of the said assignee, its successors, legal representatives and assigns.

Date 3-17-89 Name of Inventor Yunik Chang

Date 3/16/89 Name of Inventor Dinesh C. Patel

Date 3-16-89 Name of Inventor Charles D. Ebert

Date _____ Name of Inventor _____

Date _____ Name of Inventor _____

Date _____ Name of Inventor _____

RECORDED
PATENT & TRADEMARK OFFICE

MAR 21 89

COMMISSIONER OF PATENTS
AND TRADEMARKS OFFICE

REEL 5056 FRAME 212

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

TO: CIOTTI & MURASHIGE
IRRELL & MANELLA
545 MIDDLEFIELD RD., STE. 200
MENLO PARK, CA 94025

RECEIVED APR 29 1988

UNITED STATES PATENT AND TRADEMARK OFFICE
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ASSIGNOR: 001 CHANG, YUNIK DOC DATE: 12/16/87
ASSIGNOR: 002 PATEL, DINESH C. DOC DATE: 12/15/87
ASSIGNOR: 003 EBERT, CHARLES D. DOC DATE: 12/15/87

RECORDATION DATE: 12/28/87 NUMBER OF PAGES 001 REEL/FRAME 4802/0996

DIGEST: ASSIGNMENT OF ASSIGNORS INTEREST

ASSIGNEE: 501 THERATECH, INC., RESEARCH PARK, 410 CHIPETA WAY, SUITE 21 9, SALT LAKE CITY, UTAH 84108, A CORP. OF UTAH

SERIAL NUMBER 7-119617 FILING DATE 11/12/87
PATENT NUMBER ISSUE DATE 00/00/00

TITLE OF INVENTION: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SK IN OR MUCOSA

INVENTOR: 001 CHANG, YUNIK
INVENTOR: 002 PATEL, DINESH C.
INVENTOR: 003 EBERT, CHARLES D.

DOCKETED TEC
For 9065-0003

Atty Dkt 9065-0003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 23 December 1987 Date

In re Application of)
YUNIK CHANG et al)
Serial No.: 119,617)
Filed: 12 November 1987)
For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA)

Group Art Unit:

Examiner: Thomas E. Ciotti (Signature)

Attention: Application Division 23 December 1987 Date

TRANSMITTAL LETTER FOR MISSING PARTS OF APPLICATION

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

In complete response to the Notice to File Missing Parts of Application Under 37 C.F.R. §1.53(d) dated 8 December 1987, attached please find: Communication regarding change in order of Inventorship;

- [X] a combined Declaration and Power of Attorney signed by the inventor(s) and the surcharge of [ ] $55.00 [X] $110.00 as set forth in 37 C.F.R. §1.16(e);
- [ ] a Declaration of Small Entity Status and a Request for Refund;
- [ ] a Petition for Extension of Time;
- [ ] a verified English translation of the application, and the $26.00 fee as set forth in 37 C.F.R. §1.17(k);
- [X] an Assignment document and the $ 7.00 Assignment Recording Fee;
- [X] other Filing fee of $340.00;
- [X] a check in the amount of $ 457.00.
- [ ] Charge $_____ to Deposit Account No. 03-1952.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 03-1952. A duplicate copy of this sheet is enclosed.

Respectfully submitted,
CIOTTI & MURASHIGE, IRELL & MANELLA

By 1 518 Thomas E. Ciotti
Thomas E. Ciotti
Registration No. 21,013

545 Middlefield Road
Suite 200
Menlo Park, CA 94025-3471
Phone No.: (415) 327-7250

080 01/11/88 119617

9065-0003
JOINT

ASSIGNMENT

THIS ASSIGNMENT, by YUNIK CHANG, DINESH C. PATEL and CHARLES D. EBERT

(hereinafter referred to as the assignors), residing at Toms River, New Jersey Murray, Utah and Salt Lake City, Utah, respectively, witnesseth:

WHEREAS, the said assignors have invented certain new and useful improvements in DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

set forth in an application for Letters Patent of the United States, ☐ having an oath or declaration executed on even date herewith; ☒ bearing Serial No. 119,617 and filed on 12 November 1987; and

WHEREAS, TheraTech, Inc., a corporation duly organized under and pursuant to the laws of Utah, and having its principal place of business at Research Park, 410 Chipeta Way, Suite 219, Salt Lake City, Utah 84108

(hereinafter referred to as the assignee) is desirous of acquiring the entire right, title and interest in and to said inventions and said application for Letters Patent of the United States, and in and to any Letters Patent or Patents, United States or foreign, to be obtained therefor and thereon:

NOW, THEREFORE, in consideration of One Dollar ($1.00) and other good and sufficient considerations, the receipt of which is hereby acknowledged, the said assignors have sold, assigned, transferred and set over, and by these presents do sell, assign, transfer and set over, unto the assignee, its successors, legal representatives and assigns, the entire right, title and interest in and to the abovementioned inventions, application for Letters Patent, and any and all Letters Patent or Patents in the United States of Ameriea and all foreign countries which may be granted therefor and thereon, and in and to any and all divisions, continuations, and continuations-in-part of said application, or reissues or extensions of said Letters Patent or Patents, and all rights under the International Convention for the Protection Of Industrial Property, the same to be held and enjoyed by the said assignee, for its own use and behoof and the use and behoof of its successors, legal representatives and assigns, to the full end of the term or terms for which Letters Patent or Patents may be granted, as fully and entirely as the same would have been held and enjoyed by the assignors, had this sale and assignment not been made.

AND for the same consideration, the said assignors hereby covenant and agree to and with the said assignee, its successors, legal representatives and assigns, that, at the time of execution and delivery of these presents, the said assignors are the sole and lawful owners of the entire right, title and interest in and to the said inventions and the application for Letters Patent above mentioned, and that the same are unencumbered and that the said assignors have good and full right and lawful authority to sell and convey the same in the manner here in set forth.

AND for the same consideration, the said assignors hereby covenant and agree to and with the said assignee, its successors, legal representatives and assigns, that the said assignors will, whenever counsel of the said assignee, or the counsel of its successors, legal representatives and assigns, shall advise that any proceeding in connection with said inventions, or said application for Letters Patent, or any proceeding in connection with Letters Patent for said inventions in any country, including interference proceedings, is lawful and desirable, or that any division, continuation or continuation-in-part of any application for Letters Patent, or any reissue or extension of any Letters Patent, to be obtained thereon, is lawful and desirable, sign all papers and documents, take all lawful oaths, and do all acts necessary or required to be done for the procurement, maintenance, enforcement and defense of Letters Patent for said inventions, without charge to the said assignee, its successors, legal representatives and assigns, but at the cost and expense of the said assignee, its successors, legal representatives and assigns.

AND the said assignors hereby request the Commissioner of Patents to issue said Letters Patent of the United States to the said assignee, as the assignee of said inventions and the Letters Patent to be issued thereon for the sole use and behoof of the said assignee, its successors, legal representatives and assigns.

RECORDED
PATENT & TRADEMARK OFFICE
DEC 28 1987

Date 12-16-87 Name of Inventor YUNIK CHANG

Date 12-15-87 Name of Inventor DINESH C. PATEL

Date 12-15-87 Name of Inventor CHARLES D. EBERT

B

PATENT
Docket No. 290652802400

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Yunik Chang et al.

Serial No.: 07/326,536

Filing Date: March 21, 1989

Patent No.: 4,983,395

Issued: January 8, 1991

For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

ASSOCIATE POWER OF ATTORNEY

Assistant Commissioner for Patents
Box Patent Extension
Washington, D.C. 20231

Dear Sir:

In the matter of the above-entitled patent, please recognize the following attorneys and agents:

Thomas E. Ciotti (Reg No 21,013)
Gladys H. Monroy (Reg No 32,430)
Paul Schenck (Reg No 27,253)
Freddie K. Park (Reg No 35,636)
Paul C. Kimball (Reg No 34,641)
Patricia M. Drost (Reg No 29,790)
Cecily Anne Snyder (Reg No 37,448)
Edward G. Durney (Reg No 37,611)
Gary A. Green (Reg No 38,474)
Harry J. Macey (Reg No 32,818)
David L. Bradfute (Reg No 39,117)
Laurie Axford (Reg No 35,053)
Catherine M. Polizzi (Reg No P40,130)
Kate H. Murashige (Reg No 29,959)
Debra Shetka (Reg No 33,309)
Thomas E. Wheelock (Reg No 28,825)
Susan K. Lehnhardt (Reg No 33,943)
James R. Shay (Reg No 32,062)
Shmuel Livnat (Reg No 33,949)
Tyler Dylan (Reg No 37,612)
Reid G. Adler (Reg No 30,988)
Antoinette F. Konski (Reg No 34,202)
Stuart P. Kaler (Reg No 35,913)
Robert Saltzberg (Reg No 36,910)
Mani Adeli (Reg No P39,585)
Sean Brennan (Reg No P39,917)

ps-51173

James C. Peacock III (Reg No P40,124) J. Michael Schiff (Reg No P40,253)

whose address is:

Morrison & Foerster
755 Page Mill Road
Palo Alto, California 94304-1018

as my associates in the above-identified application to inspect the file, to prepare and file amendments, to inspect and make copies thereof and of any papers in any appellate and *inter partes* proceedings in which the application or patent issued thereon may be or become involved, and generally to conduct all business in the United States Patent and Trademark Office connected therewith including the application for extension of the patent term of the patent issued thereon.

Please direct all communications concerning this matter to:

Antoinette F. Konski
Morrison & Foerster
755 Page Mill Road
Palo Alto, California 94304-1018

Telephone: (415) 677-6113
Facsimile: (415) 494-0792

Dated: November 21, 1995

TheraTech, Inc.
Assignee of Record

By: Charles D. Ebert
Name: Charles D. Ebert
Title: Senior Vice President R&D

417 Wakara Way, Suite 100
Salt Lake City, Utah 84108

CERTIFICATE UNDER 37 CFR Section 3.73(b)

Applicants: Yunik Chang, Dinesh C. Patel, and Charles D. Ebert;

For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA, U.S. Patent No. 4,983,395, issued January 8, 1991, filed as U.S. Application No. 07/326,536, on March 21, 1989, a continuation-in-part of U.S. Serial No. 07/119,617, filed November 12, 1987, now U.S. Patent No. 4,849,224, issued July 18, 1989;

and TheraTech, Inc. a corporation organized under the laws of the state of Delaware and having a place of business at 417 Wakara Way, Suite 100, Salt Lake City, Utah, 84108;

certifies that it is the assignee of the entire right, title and interest in the patent identified above by virtue of:

an assignment from the inventors to TheraTech, Inc., recorded on March 21, 1989, on Reel 5056, Frame 0212, and by virtue of an assignment for U.S. Patent No. 4,849,224, recorded on December 28, 1987, on Reel 4802, Frame 0996.

The undersigned has reviewed all the documents in the chain of title of the patent application identified above and, to the best of undersigned's knowledge and belief, title is in the assignee identified above. The undersigned (whose title is supplied below) is empowered to act on behalf of the assignee.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: November 21, 1995

Name: Charles D. Ebert

Title: Senior Vice President, Research and Development

Signature: Charles D. Ebert

pa-51178

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

OCT 6 1989
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TO: IRELL & MANELLA
545 MIDDLEFIELD ROAD, STE. 200
MENLO PARK, CA 94025-3471

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE U.S. PATENT AND TRADEMARK OFFICE ON THE REEL AND FRAME NUMBER REFERENCED BELOW. A DIGEST OF THE DOCUMENT HAS ALSO BEEN MADE AND APPEARS IN THE OFFICE'S RECORDS AS SHOWN:

ASSIGNOR: 001 CHANG, YUNIK DOC DATE: 03/17/89
ASSIGNOR: 002 PATEL, DINESH C. DOC DATE: 03/16/89
ASSIGNOR: 003 EBERT, CHARLES D. DOC DATE: 03/16/89

RECORDATION DATE: 03/21/89 NUMBER OF PAGES 001 REEL/FRAME 5056/0212

DIGEST: ASSIGNMENT OF ASSIGNORS INTEREST

ASSIGNEE: 501 THERATECH, INC., RESEARCH PARK, 410 CHIPETA WAY, STE. 219 , SALT LAKE CITY, UT 84108, A CORP. OF UT

SERIAL NUMBER 7-326536 FILING DATE 03/21/89
PATENT NUMBER ISSUE DATE 00/00/00

TITLE OF INVENTION: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SK IN OR MUCOSA

INVENTOR: 001 CHANG, YUNIK
INVENTOR: 002 PATEL, DINESH C.
INVENTOR: 003 EBERT, CHARLES D.

DOCKETED TEC
9065-0003 20

#7.02 578

Attorney Docket No. 9065-0003.2

IRELL & MANELLA
545 Middlefield Road, Suite 200
Menlo Park, California 94025-3471

07/326536

APPLICATION TRANSMITTAL LETTER

Honorable Commissioner of Patents and Trademarks
Washington, D. C. 20231

Sir:

Transmitted herewith for filing is the patent application

of Yunik Chang, Dinesh C. Patel, Charles D. Ebert

for DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

Enclosed are:

- [X] 2 sheet(s) of [ ] formal [X] informal drawing(s). (3 sets)
- [ ] A claim for foreign priority under 35 U.S.C. §119/363 in [ ] a separate document [ ] the declaration.
- [ ] A certified copy of the priority document.
- [ ] An Associate Power of Attorney.
- [ ] _____ verified statement(s) of small entity status.

The declaration of the inventor [X] is enclosed [ ] will follow.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label No. RB100193775
Date of Deposit: 3-21-89
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail" Post Office to Addressee service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.
DOROTHY M. PAUL
(Typed or Printed Name of Person Mailing Paper or Fee)
Dorothy M. Paul
(Signature of Person Mailing Paper or Fee)

The fee has been calculated as follows:

A. Basic Application Fee			$ 340.00
B. Total Claims 6 minus 20 = 0	x $ 12.00	=	$ -0-
C. Independent Claims 1 minus 3 = 0	x $ 34.00	=	$ -0-
D. If multiple dependent claims present, add	$ 110.00	=	$ -0-
E. Total Application Fee (Total of A, B, C, & D)		=	$ 340.00
F. If verified statement of small entity status is enclosed, fifty percent reduction of Total Application Fee (50% x E)		=	$ -0-
G. Application Fee Due (E minus F)		=	$ 340.00
H. Assignment Recording Fee of $7.00 if assignment document enclosed.		=	$ 7.00
I. TOTAL FEE (G plus H)		=	$ 347.00

[X] A check in the amount of $ 347.00 is attached.

[ ] Charge $_____ to Deposit Account No. 03-1952.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 03-1952. A duplicate copy of this sheet is enclosed.

*Attention: Assignment Branch

1 518 7.00 CK

By Thomas E. Ciotti
Thomas E. Ciotti
Registration No.: 21,013

93032427

Phone No.: 415/327-7250

Attorney Docket No. 9065-0003.20

ASSIGNMENT

JOINT

THIS ASSIGNMENT, by * Yunik Chang, Dinesh C. Patel, Charles D. Ebert,

(hereinafter referred to as the assignors), residing at Toms River, New Jersey; Murray, Utah; Salt Lake City, Utah and Salt Lake City, Utah respectively, witnesseth:

WHEREAS, the said assignors have invented certain new and useful improvements in DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

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Date 3-17-89 Name of Inventor Yunik Chang

Date 3/16/89 Name of Inventor Dinesh C. Patel

Date 3-16-89 Name of Inventor Charles D. Ebert

Date _____ Name of Inventor _____

Date _____ Name of Inventor _____

Date _____ Name of Inventor _____

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PATENT & TRADEMARK OFFICE

MAR 21 89

COMMISSIONER OF PATENTS
AND TRADEMARKS OFFICE

REEL 5056 FRAME 212

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

TO: CIOTTI & MURASHIGE
IRRELL & MANELLA
545 MIDDLEFIELD RD., STE. 200
MENLO PARK, CA 94025

RECEIVED
APR 29 1988

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

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ASSIGNOR: 001 CHANG, YUNIK	DOC DATE: 12/16/87
ASSIGNOR: 002 PATEL, DINESH C.	DOC DATE: 12/15/87
ASSIGNOR: 003 EBERT, CHARLES D.	DOC DATE: 12/15/87

RECORDATION DATE: 12/28/87 NUMBER OF PAGES 001 REEL/FRAME 4802/0996

DIGEST: ASSIGNMENT OF ASSIGNORS INTEREST

ASSIGNEE: 501 THERATECH, INC., RESEARCH PARK, 410 CHIPETA WAY, SUITE 21 9, SALT LAKE CITY, UTAH 84108, A CORP. OF UTAH

SERIAL NUMBER 7-119617 FILING DATE 11/12/87
PATENT NUMBER ISSUE DATE 00/00/00

TITLE OF INVENTION: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SK IN OR MUCOSA

INVENTOR: 001 CHANG, YUNIK
INVENTOR: 002 PATEL, DINESH C.
INVENTOR: 003 EBERT, CHARLES D.

DOCKETED TEC
For 9065-0003

Atty Dkt 9065-0003

[redacted]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 23 December 1987 Date

In re Application of)
YUNIK CHANG et al)
Serial No.: 119,617)
Filed: 12 November 1987)
For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA)

Group Art Unit:
Examiner: Thomas E. Ciotti (Signature)
Attention: Application Division 23 December 1987 Date

TRANSMITTAL LETTER FOR MISSING PARTS OF APPLICATION

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

In complete response to the Notice to File Missing Parts of Application Under 37 C.F.R. §1.53(d) dated 8 December 1987, attached please find: Communication regarding change in order of Inventorship;

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Respectfully submitted,
CIOTTI & MURASHIGE, IRELL & MANELLA

By Thomas E. Ciotti
Thomas E. Ciotti
Registration No. 21,013

545 Middlefield Road
Suite 200
Menlo Park, CA 94025-3471
Phone No.: (415) 327-7250

080 01/11/88 119617

9065-0003
JOINT

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RECORDED
PATENT & TRADEMARK OFFICE
DEC 28 1987

Date 12-16-87 Name of Inventor YUNIK CHANG

Date 12-15-87 Name of Inventor DINESH C. PATEL

Date 12-15-87 Name of Inventor CHARLES D. EBERT

United States atent [19]
Chang et al.

[11] **Paten. .Number: 4,983,395**
[45] **Date of Patent: * Jan. 8, 1991**

[54] **DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA**

[75] Inventors: **Yunik Chang**, Toms River, N.J.; **Dinesh C. Patel**, Murray; **Charles D. Ebert**, Salt Lake City, both of Utah

[73] Assignee: **TheraTech Inc.**, Salt Lake City, Utah

[*] Notice: The portion of the term of this patent subsequent to Jul. 18, 2006 has been disclaimed.

[21] Appl. No.: **326,536**

[22] Filed: **Mar. 21, 1989**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 119,617, Nov. 12, 1987, Pat. No. 4,849,224.

[51] **Int. Cl.**[5] **A61F 13/02**
[52] **U.S. Cl.** **424/448**; 424/449; 424/447; 424/434
[58] **Field of Search** 424/448, 449, 434

[56] **References Cited**

U.S. PATENT DOCUMENTS

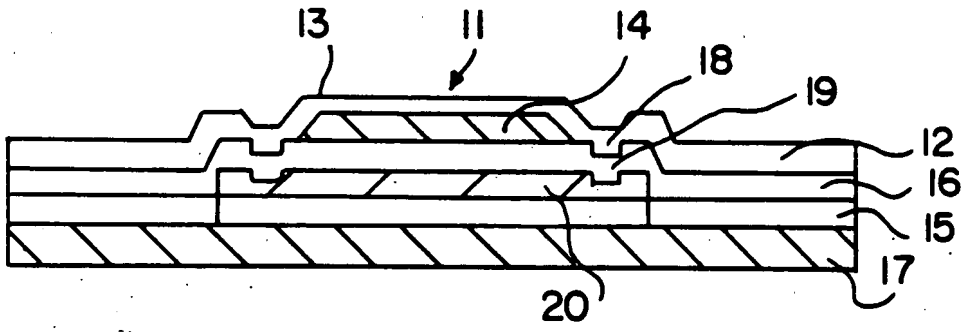
4,849,224 7/1989 Chang et al. 424/434

Primary Examiner—Merrell C. Cashion, Jr.
Assistant Examiner—Leon R. Horne
Attorney, Agent, or Firm—Irell & Manella

[57] **ABSTRACT**

A transdermal drug delivery device comprising a drug formulation-containing reservoir defined by a backing layer and a drug-permeable membrane layer, a peelable inner liner that underlies the reservoir and a portion of the backing/membrane outwardly of the reservoir periphery, an adhesive layer that underlies the inner liner and outwardly extending portions of the membrane/-backing layers, and a peelable release liner layer that underlies the adhesive layer with a first permanent heat seal between the backing and the membrane about the perimeter of the reservoir and another concentric peelable (impermanent) heat seal between the membrane and the inner liner positioned underlying and at a radius not less than the first permanent heat seal, the heat seals and peelable barrier layer providing barriers that isolate the drug formulation from the adhesive.

6 Claims, 2 Drawing Sheets



Application for Patent Extension
Patent No. 4,983,395
Atty Dkt.: 290652802400
Appendix C

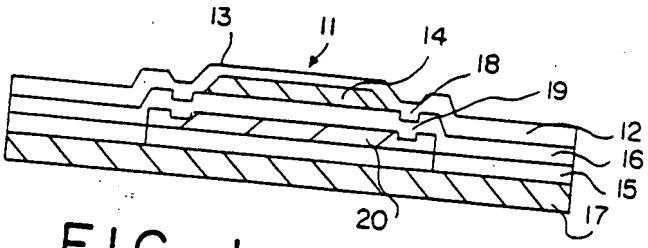


FIG. 1

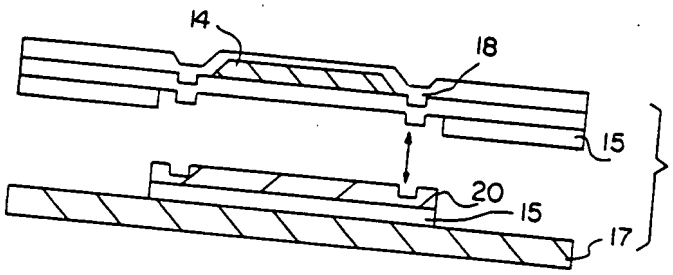


FIG. 2

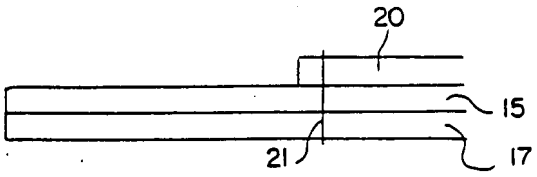


FIG. 3

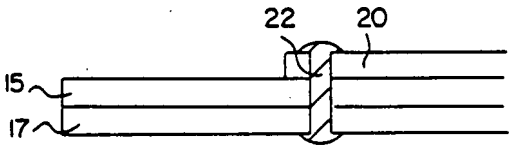


FIG. 4

DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of copending U.S. application Ser. No. 119,617 filed 12 Nov. 1987, now U.S. Pat. No. 4,849,224.

TECHNICAL FIELD

This invention is in the field of transdermal/ transmucosal administration of active agents (drugs). More particularly it relates to a device for achieving such administration comprising an active agent-containing reservoir and an adhesive layer for affixing the device to the skin or mucosa in which the adhesive layer is peripheral to the path of the active agent to the skin or mucosa and is protected from degradation by the components of the reservoir by a multiplicity of heat seals.

BACKGROUND OF THE INVENTION

There are many patents describing devices for administering drugs through the skin or mucosa. These devices are commonly in the form of a laminated composite that includes a reservoir layer containing the drug, a pressure sensitive adhesive layer for attaching the composite to the skin, and a backing layer that forms the upper layer of the device. Depending upon the particular drug and drug formulation involved, the reservoir layer may be a matrix in which the drug formulation is dispersed or a layer in the form of a walled container which holds the drug formulation. Container-type reservoirs are often formed as a pocket between the backing layer and a drug-permeable basal membrane through which the drug passes to the skin. The pressure sensitive adhesive layer normally underlies the membrane and the drug also passes through it on its way to the skin.

Devices having container-type reservoirs with underlying pressure sensitive adhesive layers have significant disadvantages when one or more components of the drug formulation that are released from the reservoir to the skin are solvents for the adhesive or otherwise adversely effect the properties of the adhesive as they pass through it to the skin. In such cases those reservoir component(s) cannot be permitted to pass through the adhesive and means must be found to isolate the adhesive from them. Further, in such devices the drug partitions into the adhesive and alters drug release characteristics over prolonged storage. The present invention provides a device design in which the adhesive is peripheral to the path of the drug formulation and is isolated from the drug formulation by a peelable barrier disc and a multiplicity of heat seals between selected layers of the device.

At least one other transdermal drug delivery device design has been proposed which involves an adhesive layer that is peripheral to the path of the drug to the skin. U.S. Pat. No. 4,573,996 describes a device that has both a drug-permeable adhesive layer in the path of the drug and a peripheral drug-impermeable adhesive layer that is not in the path of the drug. The purpose of the peripheral adhesive layer is to provide a site for handling the device which avoids the risks of altering the drug path or contaminating the fingers with drug. FIG. 6 of the patent shows a multi-layer laminated composite composed of (1) a backing layer, (2) a drug permeable membrane underlying the backing that forms with the backing a pocket that serves as a drug-containing reservoir, (3) a drug-permeable adhesive layer directly underlying the membrane, (4) a ring-shaped drug-impermeable adhesive layer adjacent and peripheral to the drug-permeable adhesive layer, and (5) a basal removable protective layer. The combination of a heat seal between the backing and the membrane at the edge of the reservoir and the peripheral drug-impermeable adhesive layer prevents radial or horizontal migration of the drug from the reservoir. This patented device is distinct from the device of the present invention in several respects .The patented device does not involve the problem of keeping drug formulation components isolated from the adhesive layer. In the patented device, the drug passes through the drug-permeable adhesive layer. There is only a single heat seal shown in the patented device. And, the single heat seal is not used to isolate the drug formulation from either adhesive layer.

The present invention is also unique in that it employs two peelable layers, a permanent heat seal and a peelable heat seal in a manner that permits the creation of a peripheral ring of adhesive when the two peelable layers are removed from the device.

DISCLOSURE OF THE INVENTION

The invention is a device for administering an active agent to the skin or mucosa of an individual comprising a laminated composite of:

(a) a backing layer;

(b) an active agent-permeable membrane, the backing layer and membrane defining

(c) a reservoir therebetween that contains a formulation of the active agent, said reservoir having a smaller periphery than the backing layer and membrane such that a portion of the backing layer and membrane extends outwardly of the periphery of the reservoir;

(d) a first peelable active agent formulation-impermeable layer that underlies the reservoir and a portion of said outwardly extending portion of the backing layer and membrane;

(e) an adhesive layer that underlies and covers the first peelable active agent formulation-impermeable layer and said outwardly extending portion of the backing layer and membrane;

(f) a second peelable active agent formulation-impermeable layer that underlies and covers the adhesive layer;

(g) a permanent heat seal about the periphery of the reservoir between the backing layer and the membrane; and

(h) a peelable heat seal between the membrane and the first peelable active agent formulation-impermeable layer located underneath and at a radius not less than that of the permanent heat seal, said permanent and peelable heat seals providing barriers to migration of components of the active agent formulation from the reservoir into the adhesive layer and said first and second peelable active agent impermeable layers being bonded together such that when the second peelable layer is removed from the device the peelable heat seal is broken and the first peelable layer and underlying portion of the adhesive layer is removed therewith.

BRIEF DESCRIPTION OF THE DRAWING

FIG. 1 is an enlarged sectional view of one embodiment of the invention.

FIG. 2 is an enlarged sectional view of the embodiment of FIG. 1 after the second and first peelable layers have been peeled off the remainder of the embodiment.

FIGS. 3 and 4 are enlarged sectional views of a portion of other embodiments depicting alternative means for affixing the first and second peelable layers together.

The drawings are not to scale and like parts are referred to by like reference numerals in the various figures.

MODES FOR CARRYING OUT THE INVENTION

The drawing shows a device, generally designated an embodiment of the invention that is designed to administer a formulation of a drug and/or a permeation enhancer that is a solvent for pressure sensitive adhesives that are commonly used in transdermal delivery devices. Device 11 is designed to place the adhesive out of the path of the enhancer-drug formulation and to prohibit radial or horizontal migration of the drug/enhancer into the adhesive. Device 11 is a laminated composite. The uppermost layer of the composite is a heat-sealable backing film 12 having an inverted, cup-shaped recess 13 that serves as a container or reservoir for a drug-enhancer formulation 14. Underlying the reservoir and all or a portion of the part of the backing layer outwardly of the reservoir is a membrane layer 16 that is permeable to the drug-enhancer formulation. An inner peel sealable liner 20 underlies the membrane layer and extends outwardly of the periphery of the reservoir. The next layer in the composite is a pressure-sensitive adhesive layer 15 that underlies the inner peel sealable liner and the portion of the backing layer that extends outwardly of the edge of the liner. Finally a peelable adhesive release liner layer 17 covers the entire underside of the assembly and forms the basal surface of the device. There are a minimum of two concentric heat seals in the composite. The first is at 18 between the membrane and the backing. It extends completely around the perimeter of the reservoir and forms a permanent seal between the backing film and membrane. The second is at 19 and is between the outer edge of the inner peel sealable liner and the membrane and forms a peelable (impermanent) seal between the membrane and inner liner. It is underneath the first heat seal and at a radius not less than that of the first heat seal. Alternatively, it may be located vertically in line with the first heat seal, but in no event should it lie inwardly of the first heat seal. These seals prevent the drug/enhancer formulation from migrating into the adhesive during storage. After the release liner is removed, the first heat seal prevents such migration during wearing. The width of the seals will usually be in the range of 0.05 cm to 1.0 cm. The peel strength between the adhesive layer and the release liner layer is greater than the force required to break the peelable seal at 19. Thus, when the release liner is peeled from the underside of the assembly the peelable seal is broken and the adhesive layer peripheral to the inner peel sealable liner is cut by the edge of that liner as the release liner and peel sealable liner 20 are removed, leaving the portion of the adhesive between liners 17 and 20 and creating a peripheral ring of adhesive underlying the membrane and backing peripheral to the reservoir (see FIG. 2). Alternatively, the release liner and the inner peel sealable liner may be bonded together (e.g., by permanent adhesive or mechanical bonding) such that removal of the release liner results in simultaneous removal of the inner liner. FIGS. 3 and 4 depict such alternative bonding means. These means are also described in Examples 5 and 6, infra. In FIG. 3 the means is a metal staple 21 that passes vertically through the first peelable layer 20, the underlying adhesive layer 15 and the second peelable (release) layer 17 just inwardly of the edge of layer 20. Correspondingly, in FIG. 4 the means is a plastic rivet 22 that is similarly passed through the three mentioned layers.

When device 11 is placed into use, the release liner layer 17 and inner liner 20 are peeled away from the underside of the device and discarded. This operation directly exposes the undersurfaces of the membrane and the peripheral ring of adhesive layer and the device can be placed on a desired site on the skin or mucosa of the individual to be treated with the active agent.

In the embodiment shown in FIGS. 1 and 2 the second impermeable heat seal is formed between the membrane and inner liner. It will be appreciated in this regard that additional heat-sealable layers could be included in the device between any of the component layers that are part of the membrane, backing or inner liner, as the case may be.

The invention device is useful when one or more of the components of the active agent formulation is incompatible with available adhesives that are useful for removably attaching elements to the skin or mucosa. The term "incompatible" is intended to mean that through physical and/or chemical interaction of the component(s) with the adhesive the adhesiveness or other desirable properties (e.g., nonirritancy) of the adhesive are significantly destroyed or impaired. The drug itself may be such a component or a carrier, solvent, skin permeation enhancing agent or other additive may be such a component. Also, this design prevents migration of drug into the adhesive which otherwise alters drug release characteristics over prolonged storage.

The backing layer 12 of the device may be composed of a single film or a plurality of films. In any event, its inner surface must be capable of being heat sealed to the membrane. One or more of the films that constitute the layer will be impermeable to components of the drug formulation contained in the reservoir. Examples of materials used as backing layers in transdermal delivery devices that may find use in the present invention are polyethylene, polypropylene, polyethylene vinylacetate, polyethylene terephthalate, and combinations thereof. The layer may include one or more metal layers and/or one or more fibrous layers.

The reservoir pocket in the backing may be formed by vacuum forming or other like methods of forming desired shapes in films.

The term "drug" as used to describe the principal active ingredient of the device intends a biologically active compound or mixture of compounds that has a therapeutic, prophylactic or other beneficial pharmacological and/or physiological effect on the wearer of the device. Examples of types of drugs that may be used in the invention device are antiinflammatory drugs, analgesics, antiarthritic drugs, antispasmodics, antidepressants, antipsychotic drugs, tranquilizers, antianxiety drugs, narcotic antagonists, antiparkinsonism agents, cholinergic agonists, anticancer drugs, immunosuppression agents, antiviral agents, antibiotic agents, appetite

suppressants, antiemetics, anticholinergics, antihistamines, antimigraine agents, coronary, cerebral or peripheral vasodilators, hormonal agents, contraceptive agents, antithrombotic agents, diuretics, antihypertensive agents, cardiovascular drugs, and the like. The appropriate drugs of such types are capable of permeating through the skin either inherently or by virtue of treatment of the skin with a percutaneous absorption enhancer. Because the size of the device is limited for patient acceptance reasons, the preferred drugs are those that are effective at low concentration in the blood stream. Examples of specific drugs are steroids such as estradiol, progesterone, norgestrel, levonorgestrel, norethindrone, medroxyprogestrone acetate, testosterone and their esters, nitro-compounds such as nitroglycerine and isosorbide nitrates, nicotine, chlorpheniramine, terfenadine, triprolidine, hydrocortisone, oxicam derivatives such as piroxicam, ketoprofen, mucopolysaccharidases such as thiomucase, buprenorphine, fentanyl, naloxone, codeine, dihydroergotamine, pizotiline, salbutamol, terbutaline, prostaglandins such as misoprostol and enprostil, omeprazole, imipramine, benzamides such as metoclopramine, scopolamine, peptides such as growth releasing factor and somatostatin, clonidine, dihydropyridines such as nifedipine, verapamil, ephedrine, pindolol, metoprolol, spironolactone, nicardipine hydrochloride, calcitriol, thiazides such as hydrochlorothiazide, flunarizine, sydononimines such as molsidomine, sulfated polysaccharides such as heparin fractions and the salts of such compounds with pharmaceutically acceptable acids or bases, as the case may be.

Depending upon the inherent permeability of the skin to the particular drug or drugs being administered by the device, the reservoir may also contain a percutaneous absorption enhancer that increases the permeability of the skin to the drug(s) and is coadministered to the skin. Examples of percutaneous absorption enhancers are those referred to in U.S. Pat. Nos. 3,989,816, 4,316,893, 4,405,616, 4,060,084, and 4,379,454 and *J Pharm Sci* (1975) 64:901-024. The formulation contained in the reservoir may also include solvent(s), gelling agents, stabilizers, and other additives. As indicated previously one or more of these components or a combination of these components is incompatible with the adhesive.

The membrane is permeable to the drug. It may be a "dense" membrane made of a material that is inherently permeable to the components of the reservoir that are to be administered to the skin or mucosa or it may be made of a microporous material whose pores are filled with a drug-permeable material including the drug-enhancer formulation itself. In the case of dense membranes, the component(s) dissolve in the material and diffuse through the material to the skin. In the case of microporous materials the component(s) diffuse through the pores to the skin. The membrane may or may not be a rate-controlling element depending upon the particular drug involved, the permeability of the skin to the drug, and the rate of delivery required to provide therapy. Examples of materials for making dense membranes are given in U.S. Pat. Nos. 3,598,122 and 4,650,484. Examples of materials for making microporous membranes are provided in U.S. Pat. Nos. 3,797,494 and 4,031,894.

The adhesive layer is composed of a pressure sensitive surgical adhesive such as those that are commonly used to affix transdermal drug delivery devices, bandages or other dressings to the skin. Examples of such adhesives are polyisobutene, natural rubber adhesives, acrylic and methacrylic adhesives, and silicone adhesives.

The release liner layer 17 and inner liner 20 may be composed of a single layer or a multiplicity of layers. They should be (1) impermeable to the components of the drug formulation that diffuse through the membrane, (2) heat-sealable in the case of the inner liner, and (3) inherently strippable or peelable or rendered so by techniques such as silicon or fluorocarbon treatment or surface treatment with a seal incompatible layer. An example of a film having such properties is Bertek 4418 Peelable Seal.

The respective components of the device may be formulated and assembled using procedures that are known in the drug formulation, transdermal device, and laminating arts. The shape of the device is not critical, and devices of preformed shapes may be assembled directly or punched, cut, or otherwise formed from large sheets of laminated composite.

The following examples further illustrate the invention. These examples are not intended to limit the invention in any manner.

EXAMPLES

Example 1

A silicone adhesive is prepared by mixing Dow Corning 355 Medical Adhesive with Dow Corning 360 Medical Fluid (10,000 cps) to provide 20% (wt/wt) Medical fluid in the final adhesive. The adhesive/medical fluid mixture is coated onto an Akrosil Biorelease release liner using a 10 mil gap casting knife and the adhesive solvent is evaporated at 80° C. for 15 min to provide a final dry adhesive coating thickness of 0.0025 inches. A peelable heat seal disc (Bertek 4418) is then die cut into a 1.375 inch diameter circular disc which is positioned onto the adhesive surface of above adhesive-coated release liner with the peelable heat seal surface facing outward. A 0.002 inch thick microporous membrane (3M, MSP-61588) is then laminated over the entire surface of the above adhesive/release liner/peelable disc structure to form a membrane/peelable disc/adhesive/release liner laminate (L1).

The backing film (Scotchpak 1012) is pressure formed to provide a 5 cm^2 surface area and a 0.4 cc volume circular shaped cup.

A gelled calcitriol/enhancer reservoir formulation is prepared by mixing sufficient amounts of calcitriol and Klucel HF ® with a 67.5%/21.75%/7.5%/3.25% (volume percent) mixture of ethanol/water/glycerine/-methyl laurate to provide a 100 ug/ml calcitriol concentration and a 1.5% Klucel HF © gel.

To fabricate a clacitriol system, 0.4 ml of the gelled calcitriol formulation is pipetted onto the microporous membrane surface of the L1 laminate coinciding with the exact center of the peelable disc underlying the membrane. The backing film is then placed over the L1 laminate such that the pre-formed cup on the backing film is situated over the drug/enhancer gel. The backing film is then heat sealed to the L1 laminate using a 0.9934 inch diameter circular heat seal die with a 0.0787 inch width heat sealing zone at 320° C. with 30 PSI pressure for 0.5 seconds. The single heat sealing step creates the permanent heat seal between the backing film and microporous membrane layers, and simultaneously forms the peelable seal between the micropo-

rous membrane and the peelable disc directly underneath the permanent seal.

The backing film is then sealed to the microporous membrane in the outer area peripheral to the drug-enhancer reservoir with a heated plate. Finally, a 20 cm^2 (overall surface area) calcitriol system is die cut from the heat sealed structure using a steel rule die.

The peel force between the silicone adhesive and the release liner is greater than the force necessary to break the peelable seal between the membrane and the peelable disc. Therefore, when the release liner is peeled the release liner exposing the 5 cm^2 microporous membrane drug-enhancer delivery surface area and creating the peripheral adhesive pattern. The in vitro steady state calcitriol skin flux is determined using the methods of Merritt and Cooper (J. Controlled Release 1:161, 1984) to be 1 ug/cm^2day.

Example 2

A membrane/peelable disc/adhesive/release liner laminate (L1) is prepared as described in Example 1 using a Scotchpak 1022 release liner in place of the Akrosil Biorelease release liner.

A pindolol-enhancer gel formulation is prepared by mixing adequate quantities of pindolol HCl and Klucel HF® with a mixture consisting of 50%/39%/10%/1% (volume percent) ethanol/water/-glycerine/glycerol monooleate to provide a gel with a final pindolol concentration of 65 mg/cc and Klucel level of 1.5% (wt/wt).

The pindolol-enhancer gel is pipetted (0.4 ml) onto the L1 laminate and a Scotchpak 1012 backing film (0.4 ml cup previously formed) is positioned over the laminate. The backing film is then heat sealed to the L1 laminate and a final system is die cut as described in Example 1. When the release liner is peeled from the system, the peel force between the adhesive and release liner is greater than the force necessary to break the peelable seal between the peelable disc and the microporous membrane. The peelable disc is thus removed from the system with the release liner, creating the peripheral adhesive and exposing the drug-enhancer delivery surface area. The in vitro pindolol skin flux from the system is determined using the methods of Merritt and Cooper, supra, to be 33 ug/cm^2/hr.

Example 3

An L1 laminate is prepared as described in Example 1 using a polyisobutylene (PIB) adhesive in place of the silicone adhesive and a Daubert C-150 release liner in place of the Akrosil Biorelease release liner. A nicardipine-enhancer gel formulation is prepared by mixing adequate quantities of nicardipine HCl and Klucel HF® with a 65%/10%/20%/5% (volume percent) mixture of ethanol/ water/glycerine/glycerol monooleate to provide a final gel with a nicardipine concentration of 150 mg/cc and a Klucel level of 1.5% (wt/wt). A nicardipine transdermal system is then prepared as described in Example 1 using the nicardipine-enhancer gel formulation.

As with the previous examples, the peel force between the PIB adhesive and the release liner is greater than the force necessary to break the peelable seal between the microporous membrane and the peelable disc. As such, the peelable disc is removed with the release liner when the release liner is peeled away from the system, simultaneously creating the peripheral adhesive pattern. The in vitro skin flux from the nicardipine system is determined using the methods described above to be 15 ug/cm^2/hr.

Example 4

The L1 laminate is prepared as described in Example 1 using 3M #93088 medical grade acrylic adhesive in place of the silicone adhesive and a silanized release liner in place of the Akrosil Biorelease release liner.

Prior to laminating the microporous membrane, the disc is fastened to the underlying release liner by using a sewing needle with a nylon thread. The needle with the nylon thread is pushed through the disc at a distance of 0.0469 inches from its peripheral edge through the underlying adhesive and release liner. This procedure is repeated in the opposite direction by first piercing the release liner followed by the disc 0.1875 inches removed from the first stitch, while still maintaining 1 mm distance to the edge of the disc. The nylon thread is pulled tight and the two ends are tied to each other forming a knot as close to the surface of the disc as possible. This stitch forms the mechanical bond between the disc and the release liner.

The 0.002 inch thick microporous membrane (3M MSP-61588) is then laminated over the entire surface of the above peelable disc/adhesive/release liner structure to form a membrane/peelable disc/adhesive/release liner laminate. This structure is used to fabricate calcitriol, pindolol and nicardipine transdermal systems as described in Examples 1, 2 and 3.

Example 5

An L1 laminate is prepared as described in Example 4 except that a mechanical bonding of the disc to the release liner is obtained by stapling the disc to the release liner. The disc is stapled 0.030 of an inch removed from the peripheral edge of the disc to the release liner by using a 0.375 inch long metal staple. Calcitriol, pindolol and nicardipine transdermal systems are then prepared as described in Examples 1, 2 and 3.

Example 6

An L1 laminate is prepared as described in Example 4 except that the mechanical bond is obtained by the use of a plastic rivet. This rivet is formed by first punching a 0.020 inch diameter hole into the disc/ adhesive/-release liner laminate. The center of this hole is 0.030 inches set back from the edge of the disc.

A thermoset polymer is then extruded into this hole and forms a mechanical bond upon cooling.

Transdermal systems are then prepared from this L1 laminate as described in the previous examples.

What is claimed is:

1. A device for administering an active agent to the skin or mucosa of an individual comprising a laminated composite of:

(a) a backing layer;

(b) an active agent-permeable membrane, the backing layer and membrane defining

(c) a reservoir therebetween that contains a formulation of the active agent, said reservoir having a smaller periphery than the backing layer and membrane such that a portion of the backing layer and membrane extends outwardly of the periphery of the reservoir;

(d) a first peelable active agent formulation-impermeable layer that underlies the reservoir and a portion of said outwardly extending portion of the backing layer and membrane;

(e) an adhesive layer that underlies and covers the first peelable active agent formulation-impermeable layer and said outwardly extending portion of the backing layer and membrane;

(f) a second peelable active agent formulation-impermeable layer that underlies and covers the adhesive layer;

(g) a permanent heat seal about the periphery of the reservoir between the backing layer and the membrane; and

(h) a peelable heat seal between the membrane and the first peelable active agent formulation-impermeable layer located underneath and at a radius not less than that of the permanent heat seal, said permanent and peelable heat seals providing barriers to migration of components of the active agent formulation from the reservoir into the adhesive layer and said first and second peelable active agent impermeable layers being bonded together such that when the second peelable layer is removed from the device the peelable heat seal is broken and the first peelable layer and underlying portion of the adhesive layer is removed therewith.

2. The device of claim 1 wherein the adhesive is incompatible with one or more of the components of the formulation that permeate through the membrane to the skin or mucosa.

3. The device of claim 1 wherein the backing layer is a laminated composite of at least one layer that is impermeable to the formulation and an inner heat-sealable layer.

4. The device of claim 1 wherein the adhesive is an acrylic adhesive, the active agent is pindolol hydrochloride, and the formulation includes ethyl alcohol and glycerol monooleate.

5. The device of claim 1 wherein the adhesive is an acrylic adhesive, the active agent is nicardipine hydrochloride, and the formulation includes ethyl alcohol and glycerol monooleate.

6. The device of claim 1 wherein the adhesive is a silicone adhesive, the active agent is calcitriol and the formulation includes ethanol, methyl laurate, and water.

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08/24/94

MAINTENANCE FEE STATEMENT

The data shown below is from the records of the Patent and Trademark Office. If the maintenance fees and any necessary surcharges have been timely paid for the patents listed below, the notation "PAID" will appear in column 10, "status" below.

If a maintenance fee payment is defective, the reason is indicated by code in column 10, "status" below. An explanation of the codes appears on the reverse of the Maintenance Fee Statement. TIMELY CORRECTION IS REQUIRED IN ORDER TO AVOID EXPIRATION OF THE PATENT. NOTE 37 CFR 1.377. THE PAYMENT(S) WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION. IF PAYMENT OR CORRECTION IS SUBMITTED DURING THE GRACE PERIOD, A SURCHARGE IS ALSO REQUIRED. NOTE 37 CFR 1.20(k) and (l).

If the statement of small entity status is defective the reason is indicated below in column 10 for the related patent number. THE STATEMENT OF SMALL ENTITY STATUS WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION.

ITM NBR	PATENT NUMBER	FEE CDE	FEE AMOUNT	SUR CHARGE	SERIAL NUMBER	PATENT DATE	FILE DATE	PAY YR	SML ENT	STAT
1	4,983,395	183	930	----	07/326,536	01/08/91	03/21/89	04	NO	PAID

If the "status" column for a patent number listed above does not indicate "PAID" a code or an asterisk (*) will appear in the "status" column. Where an asterisk (*) appears, the codes are set out below by the related item number. An explanation of the codes indicated in the "status" column and as set out below by the related item number appears on the reverse of the maintenance fee statement.

ITM NBR	ATTY DKT NUMBER
1	9065000320

DIRECT THE RESPONSE TOGETHER WITH ANY QUESTIONS ABOUT THIS NOTICE TO:
COMMISSIONER OF PATENTS AND TRADEMARKS, BOX M. FEE, WASHINGTON, DC 20231

Application for Patent Extension
Patent No. 4,983,395
Atty Dkt.: 290652802400
Appendix D

MAINTENANCE FEE STATEMENT
STATUS CODES AND DEFINITIONS

CODE	DEFINITION
	IN REGARD TO THE MAINTENANCE FEE PAYMENT(S)
F160	The maintenance fee has already been paid. A refund of the payment has been scheduled to be sent to the fee address of record.
F161	The maintenance fee payment will not be accepted because it has been tendered too early. See 37 CFR 1.362. A refund of the payment has been scheduled.
F162	The maintenance fee payment does not properly identify the patent for which payment is to be made in accordance with 37 CFR 1.366(c). Either the U. S. application serial number or the patent number has been omitted. Both numbers are necessary to ensure proper crediting of the maintenance fee to the desired patent.
F163	The maintenance fee payment based upon certificate of mailing procedures is untimely, since it is not in compliance with the requirements of 37 CFR 1.8.
F164	The maintenance fee payment based upon "Express Mail" procedures is untimely since it is not in compliance with the requirements of 37 CFR 1.10.
F165	The maintenance fee and surcharge payment are not accepted because they have been submitted with the payment of fees for other purposes. See 37 CFR 1.366(e). A refund of the payment has been scheduled.
F166	The maintenance fee payment is not accepted because it is not immediately negotiable in the United States for the full payment of the required fee. Payment should be made in U. S. specie, Treasury notes, national bank notes, post office money orders or by certified check. See 37 CFR 1.23. The payment is returned herewith.
F167	The check or deposit account authorization is not accepted because it is unsigned. It is returned herewith.
F168	The payment received or the balance in the deposit account authorized for payment is insufficient to cover payment of the maintenance fee and surcharge, if any. Any payments accepted have been applied in accordance with the provisions of 37 CFR 1.366(e).
F169	The payment is in excess of the amount required. A refund has been scheduled.
	IN REGARD TO THE STATEMENT OF SMALL ENTITY STATUS
E180	A signature to the small entity statement is omitted.
E181	A small entity statement from each joint inventor has not been received.
E182	A small entity statement from the assignee or licensee has not been received.
E183	The requirements for filing as an independent inventor have not been met. See 37 CFR 1.9(c).
E 184	The requirements for filing as a small business concern have not been met. See 37 CFR 1.9(d).
E185	The requirements for filing as a nonprofit organization have not been met. See 37 CFR 1.9(e).
E186	The small entity statement was not verified by an oath or a declaration.

14 March 1990

E

Atty Dkt: 9065-0003.20
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:
YUNIK CHANG et al.
Serial No.: 07/326,536 Group Art Unit: 158
Filed: 21 March 1989 Examiner: L. Horne
For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

TERMINAL DISCLAIMER

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

TheraTech, Inc., having an address at Research Park, 410 Chipeta Way, Suite 219, Salt Lake City, Utah 84108, U.S.A., is the assignee of all right, title, and interest in the above-captioned application, Serial No. 07/326,536, filed 21 March 1989, for "DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA" by virtue of an assignment recorded 21 March 1989 on Reel 5056, Frame 0212, and of U.S. Patent Number 4,849,224, filed 12 November 1987, directed to "DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA", by virtue of an assignment recorded 28 December 1987, on Reel 4802, Frame 0996.

TheraTech, Inc. hereby disclaims the terminal part of any patent granted on the subject patent application which would extend beyond 18 July 2006, the term of United States Patent No. 4,849,224, and hereby agrees that any

patent so granted on said application shall be enforceable only for and during such period that legal title to said patent shall be the same as legal title to United States Patent No. 4,849,224; this agreement to run with any patent granted on the subject patent application and to be binding upon the grantee, its successors, and assigns.

Petitioner does not disclaim any terminal part of any patent granted on the subject patent application prior to the expiration date of the full statutory term as presently shortened by any terminal disclaimer of United States Patent No. 4,849,224 in the event that it later: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321(a), has all claims canceled by a reexamination certificate, or is otherwise terminated prior to the expiration of its statutory term as presently shortened by any terminal disclaimer, except for the separation of legal title stated above.

Respectfully submitted,

THERATECH, INC.

By: _____
DINESH C PATEL

Title: PRESIDENT

Date: 3/8/90

das/9065-0003/20/termdisc1

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Date	Subject Matter	Activity	Comments
11/28/89	IND	Submission to FDA	Submission by TheraTech of IND pursuant to Section 505(i)
11/28/89	IND	IND received	IND received by FDA
12/01/89	IND	Letter from FDA	Receipt of IND acknowledged and IND # 34,028 assigned
01/25/90	IND	FDA letter	Request for additional information
08/20/90	IND	FDA letter	Request for formal submission o f01/20/90 FDA request for additional information
06/14/91	IND	FDA letter	FDA's comments relation to chemistry portion of submission
09/28/94	NDA 20-489	NDA 20-489 original submission	Submission under Section 505(b) for product Androderm®
10/5/94	NDA 20-489	Letter from FDA	Acknowledge receipt on 9/30/94 of NDA application and provides reference No. NDA 20-489
12/20/94	NDA 20-489 Amendment	Submission to FDA	Supplemental Submission
03/02/95	NDA 20-489 Amendment	Submission to FDA	Supplemental Submission
03/30/95	NDA 20-489 Amendment	Submission to FDA	Supplemental Submission
03/31/95	NDA 20-489 Amendment	Submission to FDA	Supplemental Submission
04/24/95	NDA 20-489 Amendment	Submission to FDA	Supplemental Submission

05/12/95	NDA 20-489 Amendment	Submission to FDA	Supplemental Submission
05/31/95	NDA 20-489 Amendment	Letter from FDA	Acknowledges review of Manufacturing/Quality Controls Section of submission and requests additional information and amendments to physician package insert for product
06/22/95	NDA 20-489	Submission to FDA	Supplemental Submission
08/16/95	NDA 20-489	Submission to FDA	Supplemental Submission
08/22/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/01/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/07/95	NDA 20-489	Letter from FDA	Requests clarification to proposed logo for Androderm®; requests use of identifier MACMIS ID # 3524 in future correspondence
09/15/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/20/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/22/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/25/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/27/95	NDA 20-489	Submission to FDA	Supplemental Submission
09/29/95	NDA 20-489	Letter from FDA	FDA APPROVAL

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PATENT
Docket No. 290652802400

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Yunik Chang et al.

Serial No.: 07/326,536

Filing Date: March 21, 1989

Patent No.: 4,983,395

Issued: January 8, 1991

For: DEVICE FOR ADMINISTERING AN ACTIVE AGENT TO THE SKIN OR MUCOSA

DECLARATION

Assistant Commissioner for Patents
Box Patent Extension
Washington, D.C. 20231

Dear Sir:

The undersigned, attorney for TheraTech, Inc. in connection with the application for patent term extension, which is the Applicant for Extension of Patent Term under 35 U.S.C. Section 156 with regard to U.S. Patent No. 4,983,395, hereby declares that:

1. I am an attorney authorized to practice before the United States Patent and Trademark Office and have general authority to act on behalf of the owner in connection with the application for patent term extension submitted herewith for U.S. Patent No. 4,983,395.

2. I have reviewed and understand the contents of the application being submitted pursuant to 35 U.S.C. Section 156 and 37 C.F.R. Section 1.740.

3. I believe the patent is subject to extension pursuant to 35 U.S.C. Section 156 and 37 C.F.R. Section 1.710.

4. I believe an extension of the length claimed is justified under 35 U.S.C. Section 156 and the applicable regulations.

5. I believe the patent of which the extension is being sought meets the conditions for extension of patent term as set forth in 37 C.F.R. Section 1.720.

6. I hereby declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any extension of patent term issued thereon.

Dated: November 22, 1995

Respectfully submitted,

By: 

Antoinette F. Konski
Registration No. 34,202

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